I   Introduction

Syphilis, one of the oldest sexually transmitted diseases (STD), is caused by the microorganism *Treponema pallidum*. The disease occurs in four stages[1]: primary, secondary, latency (early and late), and tertiary. Syphilis in the primary and secondary (P & S) stages is considered new or incident infection[2], while other stages are considered prevalent infection (1-5).

Syphilis has been and remains a public health problem in Nashville and Davidson County, Tennessee (will be referred to as "Nashville" or "Davidson County" in the following text). Since the initial release of <u>Epidemiology of Primary and Secondary Syphilis in Nashville and Davidson County, Tennessee</u> (6) in October 1998, this community has continued to face an increased rate of P & S syphilis until 1999.

From 1995 to 1996, the incidence of primary and secondary syphilis almost doubled in Nashville, from 18.2 to 36.1 cases per 100,000 persons. This dramatic increase reversed a five-year period of a declining syphilis incidence trend in Nashville. This increase continued in 1997,1998, and 1999. Although data have showed that the number of P & S syphilis cases reported in 2000 decreased 23% from the previous year, the incidence rate in 2000 is still significantly higher than that of the pre-epidemic period of 1994-1995. Clearly, Nashvillians are still experiencing a syphilis epidemic (6, 7).

The current syphilis epidemic is of tremendous economic and health consequence in Nashville. The estimated cost for the identification and treatment of syphilis patients at STD clinics in the United States was $745.32 per case in 1999 dollars (8, 9). If applied to the 2,455 cases of P & S syphilis in Nashville between 1988 and 2000, this estimate would be $1.83 million (1999 US $). If not treated, syphilis causes reproductive health problems, pregnancy-related problems, neurological problems, and cardiovascular complications. It also facilitates the transmission of HIV infection (8). The potential health burden is phenomenal.

Fighting syphilis and creating an STD-free community requires an effective control and prevention program. A better understanding of this epidemic is crucial to program development. Using epidemiological data to target population-level intervention is important to syphilis control and prevention in Nashville. It is for these reasons that this document was produced.

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[1] In addition to the four stages of the disease, there is congenital syphilis. Congenital syphilis is the result of the passage of *T. Pallidum* across the placenta to the fetus. It can occur during any stage of syphilis but risk is much higher with P & S syphilis during pregnancy (4, 5).
[2] We considered "early latent" in this report as prevalent infection because "early latent" is defined by the U.S. Public Health Service as 1 year from onset of infection (2).

The objective of this document, the second part of the investigative report, is to examine risk factors associated with the epidemic to be used to inform and direct the syphilis prevention and control efforts throughout Nashville.

The risk factors examined in the following sections are:

1. The relationship between sex and drug related criminal behaviors and syphilis infections;
2. Population factors, including population's sexual behaviors;
3. Health system issues;
4. Public health efforts; and
5. Biological and biomedical factors.

II.   The Relationship Between Sex and Drug Related Criminal Behavior and Syphilis Infections

Syphilis is a behavior-linked disease that results mainly from unprotected sex. At least eight factors influence the distribution and trends of syphilis: 1) biologic factors; 2) sexual behaviors; 3) biomedical factors; 4) availability of and access to health care; 5) health care seeking behaviors; 6) public health efforts to prevent and control syphilis; 7) population factors; and 8) socio-cultural factors (4).

Of these factors, sexual behavior, population factors, and socio-cultural factors have been examined by numerous studies (8, 10, 11, 12). Literature suggests that the most recent epidemics of syphilis in the United States during 1985-1990 have been linked to the use of illegal drugs, especially crack cocaine, and behaviors, such as the exchange of sex for drugs, known to occur in crack houses (12).

A study from Connecticut provides quantitative evidence that a syphilis epidemic was related to an increase in drug-related prostitution, particularly cocaine-related prostitution. Women incarcerated on drug or prostitution charges had extremely high rates of syphilis - in the range of 7% to 14% (10). Sex workers and their clients represent traditional "core" transmitters of STDs (8). It is estimated that one third of persons having sexual contact with an untreated case of primary and secondary syphilis will acquire the disease (12). In addition to unprotected sex with multiple partners, female sex workers also are likely to have other factors that increase their risk for STDs, such as intravenous drug use, a history of being victims of sexual abuse and violence, and inadequate access to health care (8).

An investigation of primary and secondary syphilis in Baltimore identified that cocaine use and the exchange of money or drugs for sex were frequently reported risk behaviors (13).   A similar pattern was documented in a syphilis epidemic in Los Angeles (14). In a critical review of 16 epidemiological studies that examined drug use, sexual behavior, and STDs, eight studies found an association between crack use and STD infections, and seven studies found STD infections to be related to use of other drugs or other methods of using cocaine (15).

The association of syphilis and crack cocaine may lead to concentrations of the disease in specific social networks and in crack houses. For example, in 1991 and 1992, a series of syphilis outbreaks in four rural towns in Texas were linked to crack users exchanging sex for drugs. Three outbreaks were concentrated in neighborhoods where crack cocaine dealers worked and where exchange of sex for drugs or money was common. All 26 cases in one outbreak were linked to a single sex worker. In a second outbreak, all 34 cases were among people frequenting a crack house, three of whom were sex workers (16).

During March 2000, the Department of Health and Wellness of Fulton County, Georgia, conducted STD/HIV outreach screenings through the use of its mobile van. One of the screenings took place in a neighborhood shopping plaza, adjacent to low-income housing projects. There was a high volume of drug activity in this area, closely tied to sex in exchange for money and drugs.   A total of 27 sex partners, suspects, and associates were screened for syphilis and HIV, resulting in 12 new cases of early syphilis being identified. Analysis of the acknowledged risk factors revealed unprotected sex with multiple partners and sex in exchange for drugs or money. Seventy percent of those screened revealed that they were having sex to support drug use (17).

Historically, the drug culture in the Nashville area is not limited to people living in poverty, but the cost of the drug habit is high enough that poor persons who are addicted have limited means of acquiring drugs.   A crack addict's first priority is to continue taking the drug, and among the poor, this is often accomplished through prostitution and drug sales (18). Although prostitution has long been a primary means of supporting drug habits among women, the combined pharmacological effect of drugs on sexuality as well as socio-cultural factors have made the exchange of sex for drugs a principle feature of the drug phenomenon (19).

Given the facts that 1) exchanging sex for drugs is a major factor in several syphilis epidemics in the United States and 2) all diseases are local, we conducted the following study to determine whether sex and drug related criminal behavior is an important contributing factor to the syphilis epidemic in Nashville.

A.   Methods

1. Study Design

This is a series of three population based case-control studies aimed at evaluating the association between sex and drug related criminal behavior and the acquisition of syphilis related to Nashville's current syphilis epidemic.

All reported cases of P & S syphilis during 1994-1998 were selected as the subjects of the study (case group). Reported gonorrhea and chlamydia cases and persons who visited MHD clinics for non-STD purposes during the same reporting period were used as sources for comparison (control groups). Drug and sex related criminal charge/arrest records[3] were used as the proxy indicators for sex and drug related criminal behavior among cases and controls. Existing data routinely collected by the Metropolitan Health Department (MHD)

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[3]For purpose of this report, "arrest" will indicate any arrest, whether it be a single event or multiple events. In the same manner, "arrest records" may indicate a single record or multiple records. "Arrest" and "arrest records" may be used interchangeably. Please note that one person can be arrested on one charge or on more than one charge.

and the Metropolitan Police Department (MPD) of Nashville and Davidson County were obtained and abstracted for each study subject.

2.   Case Selection

All reported primary and secondary syphilis cases in Nashville residents between January 1, 1994 and December 31, 1998 were selected as cases. By definition, all cases are newly diagnosed cases within the study period. A primary syphilis case is defined as a case in which either: 1) a lesion was present at the time of examination and typical spirochetes were seen on dark-field microscopy of the lesion exudate or 2) a lesion was present and a treponemal confirmatory test for syphilis was reactive. Secondary syphilis case is defined as a case with clinical signs (i.e., rash, condyloma lata, generalized lymphadenopathy) noted at the time of presentation and a reactive treponemal confirmatory test for syphilis.

3.   Control Selection

a.   STD control group

Any chlamydia trachomatis case reported to MHD that occurred in a Nashville resident between January 1, 1994 and December 31, 1998 and who matched a syphilis case by gender (male, female), race (black, white, and other), and age (plus or minus 3 years of the case's age) were selected as STD controls. Gonorrhea cases were selected in the same way. It is noted that literature suggests that gonorrhea patients reported cocaine use and sex with prostitutes nearly as frequently as did syphilis patients (10). The selection of gonorrhea controls will help provide useful information for Nashville's STD control.

b.   Non-STD control group

Any person ten years old or above who visited the MHD clinics for a non-STD purpose between January 1, 1994 and December 31, 1998 and who matched a syphilis case by gender (male, female), race (black, white, and other), and age (plus or minus three years of case's age) was selected as a non-STD control. Co-infections of syphilis-chlamydia, syphilis-gonorrhea, syphilis-chlamydia-gonorrhea were considered as syphilis cases and excluded from the control selection list (the number of co-infections was minimal). All duplicates for cases and controls were checked and excluded. Two non-STD controls were selected to match each case, if possible, to increase statistical power.

4. Data Collection

Exposure data (criminal charge/arrest[4]) were collected from the MPD computerized database at the Nashville Metropolitan Public Safety Information System. Data abstraction was conducted between August 1998 and July 1999 by trained epidemiologists and researchers. Besides matching with the name; age, gender, race, and address were used to ensure the correct match of each individual selected for the study. The charge/arrest records were printed. A data abstract form designed for this study was used to abstract all criminal charge/arrest records.   Charges/arrests were classified into sex related, drug related, and other charges/arrests. To be able to analyze the trend in time, sex and drug related charges/arrests were further grouped into nine intervals according to the diagnosis date of the underlying disease: one month, six months, one year, two years, three years, four years, five years, five plus years prior to the diagnosis date, and five weeks after diagnosis date.

An audit of abstracted data was performed to ensure the accuracy of data abstraction. The audit consisted of two steps: 1) two investigators independently visually inspected the abstracted data for obvious errors and completeness of data; and 2) three investigators independently checked data for accuracy. Ten percent of data were randomly selected to check from the computer information system to computer printout, from the computer printout to the abstract form, and from the abstract form to the exposure database respectively. This process detected and corrected an average of 4.2% errors. Prior to statistical analysis, charge/arrest data were checked for illogical and mathematical errors by a computer program. This was done for the entire study database (all study subjects including cases and controls) and was repeated each time that a data correction was made to the database.

The study proposal was approved by the MHD Institutional Review Board. Because the data used in this study were legally collected by government agencies, informed consent was waived. Subjects' confidentiality was assured by following the MHD confidentiality policies and procedures.

5.   Statistical Methods

a.   Data analysis

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[4] The MPD database indicated that the subjects (both cases and controls combined) were arrested for more than 100 different charges. Drug related criminal arrests include charges for 1. possession of a controlled substance, 2. public intoxication, 3. drug: cocaine, 4. narcotic equipment, 5. paraphernalia possession (drug related), 6. dangerous drugs, 7. drugs cocaine, selling, 8. driving under the influence, 9. drug offence, simple, 10. drug, counterfeit, and 11. other drug related offenses. Sex related criminal arrests included charges for 1. kidnapping a minor to sexually assault, 2. prostitution, 3. rape, aggravated, and 4. other sex related offenses.

Characteristics and criminal charge/arrest records of the reported P & S syphilis cases were presented by descriptive statistics. Trend over time was analyzed by comparing cases diagnosed before the epidemic (1994 - 1995) and those diagnosed during the epidemic (1996 - 1998). Standard statistical procedures, t-test[5], ANOVA[6], or chi-square test[7] were applied for comparison tests.

Exposure data were analyzed qualitatively (had charge/arrest record versus no charge/arrest record) and quantitatively using the actual number of charges. Association of disease and exposure was estimated by the odds ratio[8] (OR) and its 95% confidence interval[9] (95% CI). Two approaches were employed in this process: 1) using all cases and controls included in the study and 2) using only matched cases and controls. The charge/arrest data collected originally was cumulative, i.e., number of charges/arrests within two years includes charges/arrests indicated in year one, number of charges/arrests within three years includes charges/arrests indicated in year one and year two, and so on. In an attempt to search for possible time-exposure-disease links, charge/arrest data were broken down into each time interval to obtain time-specific odds ratios. Significance of an odds ratio was tested by Mantel-Haenszel chi-square test in univariate analysis, and by the Wald's test in the logistic regression analysis (a multivariate approach). Use of logistic modeling enabled effects of each variable included in the model to be adjusted simultaneously, and thus provided more information in the analysis of relationship between the disease and the exposure. For the general population (all study subjects included), parameter estimation was based on generalized estimating equations (GEE). For case-control matching data, it was based on conditional logit method.

Statistical significance level was set at 95% confidence ($\alpha = 0.05$).

b.   Matching of cases and controls

Originally, the protocol called for 1:2 case/control ratio for each control group. The resulting control groups, however, were smaller than expected. The final case/control ratio, therefore, was redefined as 1:1, with no change to the

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[5] The t-test uses a statistic to test whether two means differ significantly, or to test linear regression or correlation coefficients (20).
[6] Analysis of Variance (ANOVA) is a statistical technique that isolates and assesses the contribution of categorical independent variables to variation in the mean of a continuous dependent variable (20).
[7] The Chi-square test is any statistical test based on comparison of a test statistic to a chi-square distribution (20).
[8] Odds ratio is the ratio of two odds. The exposure odds ratio for a set of case control data is the ratio of the odds in favor of exposure among the cases to the odds in favor of exposure among noncases (control) (20).
[9] Confidence interval is the computed interval with a given probability, e.g., 95%, that the true value of a variable such as a mean, proportion, or rate is contained within the interval (20).

matching criteria (same gender and race, and age within a 3-year range). A match was conducted between the syphilis group and the three control groups individually. Thus, the three matched groups were not expected to be identical. The matching process was random and computerized. For each case, all available subjects in the particular control group were examined for eligibility based on the matching criteria, then one of these eligible controls was randomly selected and the matched pair (one case and one control) were removed per the computer program before the next matching. No replacement was allowed, neither in the case group, nor in the control groups.

c.   Tools

Statistical Analysis System (SAS Institute, Cary, NC, SAS-PC 8.0) was used to conduct mathematical quality assurance, data processing, matching, and statistical analysis.   All graphics were produced in Microsoft Excel (Version 97 SR-2).

B. Findings

1. Distribution of Cases That Had Criminal Arrest Records

a.   Overview

A total of 803 cases of P & S syphilis were confirmed and reported to the MHD during 1994 - 1998. Eight hundred and two cases[10] were selected for the study. As shown in Table 1 on the next page and Figure 1 on the page 10, 71.6% of the cases had criminal charge/arrest records, 12.3% had sex related charges/arrests, and 38.9% had drug related charges/arrests.
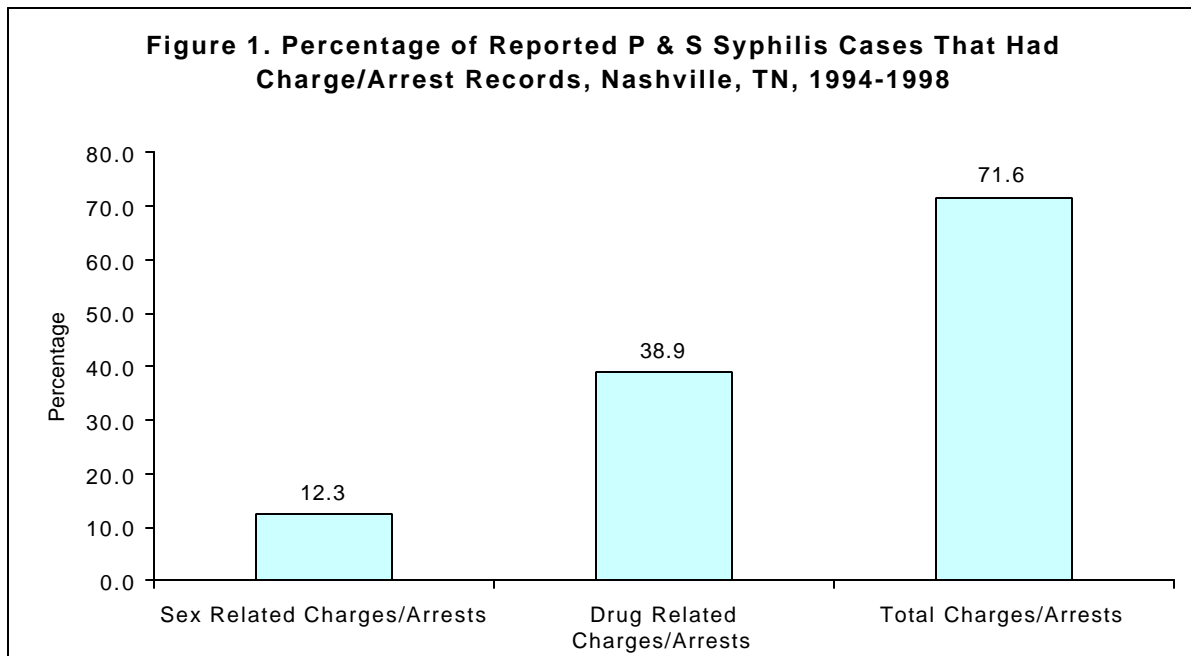
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[10] One case in 1995 was excluded from the study because it was difficult to determine if this case is a duplicated case or a re-infected case.

Table 1.   Number and Percentage of P & S Syphilis Cases That Had Criminal Charges/Arrest Records by Age, Gender, Race and Race/Gender, Nashville, TN, 1994-1998

	Sex Related Charges/Arrests (% in parenthesis)	Drug Related Charges/Arrests (% in parenthesis)	Total Charges/Arrests (% in parenthesis)	Total Cases
Age (years)				
Less than 20 Years	1 (0.1%)	6 (0.8%)***	27 (3.4%)***	62 (7.7%)
20-29 Years	21 (2.6%)	73 (9.1%)	160(20.0%)	221 (27.6%)
30-39 Years	51 (6.4%)	144 (18.0%)	231 (28.8%)	309 (38.5)
40-49 Years	21 (2.6%)	65 (8.1%)	114 (14.2%)	152 (19.0)
50 + Years	5 (0.6%)	24 (3.0%)	42 (5.2%)	58 (7.2%)
Gender				
Male	45 (5.6%)	208 (25.9%)***	332 (41.4%)***	423 (52.7%)
Female	54 (6.7%)	104 (13.0%)	242 (30.2%)	379 (47.3%)
Race				
Black	76 (9.5%)***	279 (34.8%)	517 (64.5%)	712 (88.8%)
White	23 (2.8%)	32 (4.0%)	55 (6.9%)	88 (11.0%)
Other	0 (0.0%)	1 (0.1%)	2 (0.2%)	2 (0.2%)
Race/Gender				
Black Female	39 (4.9%)***	85 (10.6%)***	212 (26.4%)***	334 (41.6%)
Black Male	37 (4.6%)	194 (24.2%)	305 (38.0%)	378 (47.1%)
White Female	15 (1.8%)	19 (2.4%)	29 (3.6%)	44 (5.5%)
White Male	8 (1.0%)	13 (1.6%)	26 (3.2%)	44 (5.5%)
Other Female	0(0.0%)	0 (0.0%)	1 (0.1%)	1 (0.1%)
Other Male	0 (0.0%)	1 (0.1%)	1 (0.1%)	1 (0.1%)
Total	99 (12.3%)	312 (38.9%)	574 (71.6%)	802 (100%)

Note: 1. The percentages in this table were calculated using 802 as the denominator.
2. Total charges/arrests includes sex related charges/arrests, drug related charges/arrests, and other charges/arrests (not shown in this table). A case could have sex related charges/arrests, drug related charges/arrests, or both.
3. Comparisons between age group, gender, race, and race/gender: *P<=0.05, **P<=0.01, ***P<=0.001.
4. Other refers to other races rather than black or white.

Table 1 also reveals that there is a statistically significant difference among age groups and between gender for drug related charges/arrests and for total charges/arrests. A statistically significant difference is also observed among races for sex related charges/arrests.   For race/gender groups, a statistically significant difference is demonstrated in sex related, drug related, and total charges/arrests.

Figure 1. Percentage of Reported P & S Syphilis Cases That Had Charge/Arrest Records, Nashville, TN, 1994-1998

b.   Age

Figure 2 on the next page reveals that syphilis cases in the 30-39 age group had the highest percentage of charge/arrest records (28.8%), followed by the 20-29 age group (20.0 %). For sex related charges/arrests, the 30-39 age group had the highest percentage (6.4%), followed by the 20-29 age group and the 40-49 age group (both 2.6%).   A similar distribution was observed in drug related arrests (the 30-39 age group: 18.0%, the 20-29 age group: 9.1%, and the 40-49 age group: 8.1%).

Figure 2. Percentage of P & S Syphilis Cases That Had Charge/Arrest Records by Age, Nashville, TN, 1994-1998
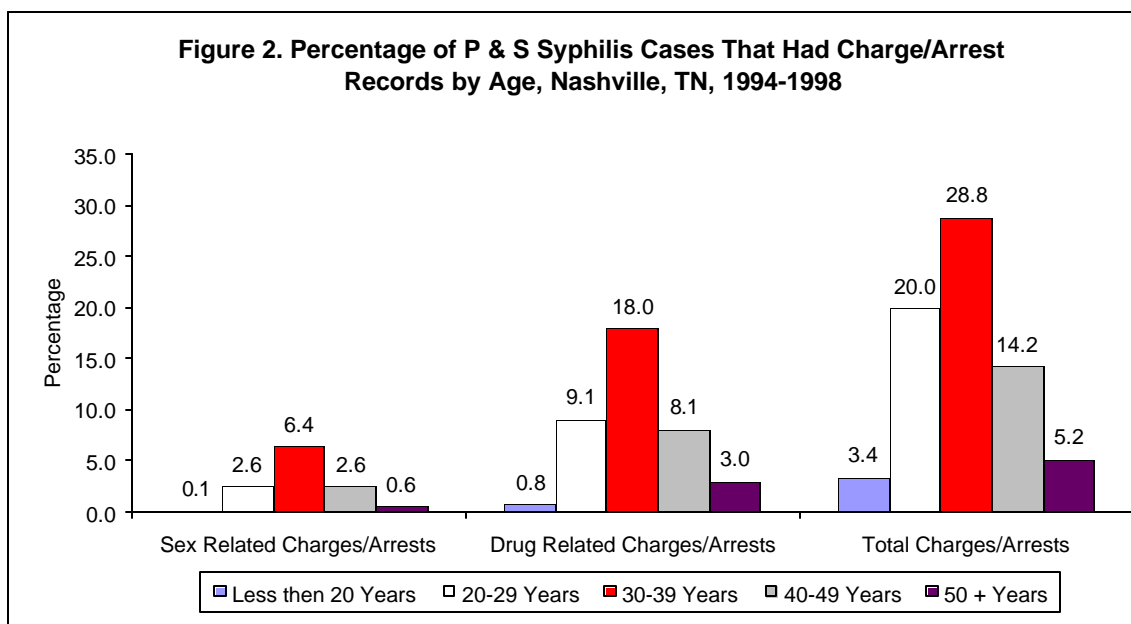
c.   Gender and race

From Figure 3, it is observed that male cases had a higher percentage of total charge/arrest records than female cases and black cases had a higher percentage of total charge/arrest records than white cases. For sex related charges/arrests, the percentage of female cases who had charge/arrest records is slightly higher than their male counterparts, and the percentage of black cases who had charge/arrest records is more than 3 times higher than that of their white counterparts. For drug related charge/arrests, the percentage of male cases who had charge/arrest records is almost twice as high as that of their
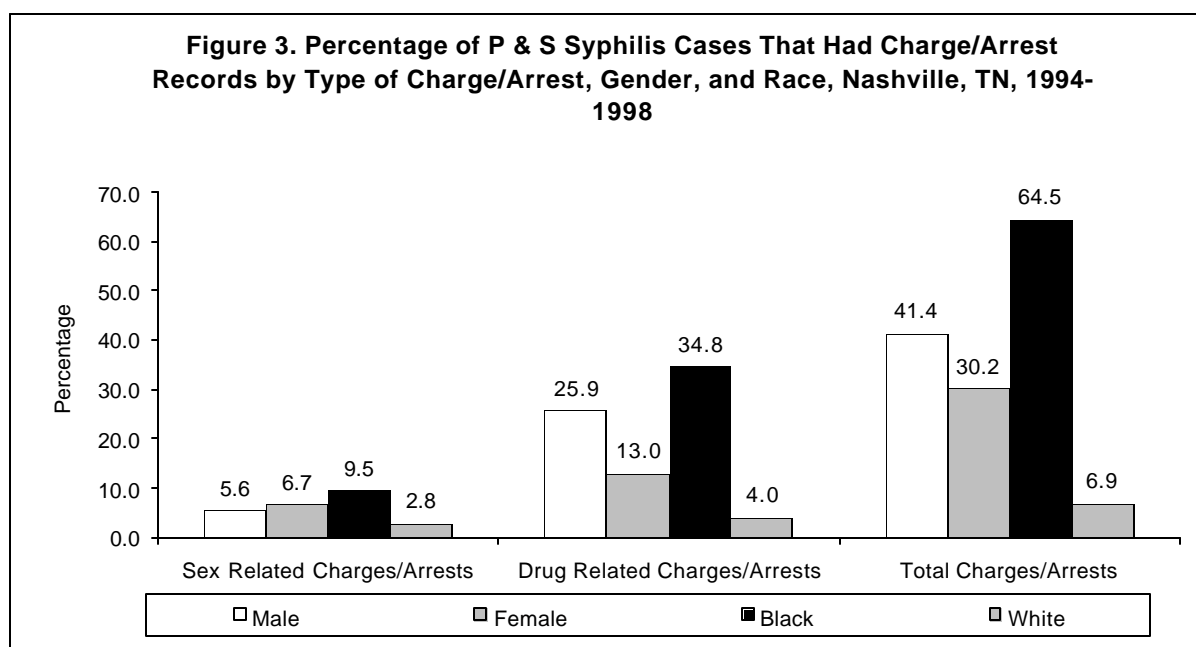
Figure 3. Percentage of P & S Syphilis Cases That Had Charge/Arrest Records by Type of Charge/Arrest, Gender, and Race, Nashville, TN, 1994-1998

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female counterparts, and the percentage of black cases who had charge/arrest records is more than eight times higher than that of white cases.

Further examining the cases by gender and race (Figure 4), it is noted that the black male cases had the highest percentage (38.0%) of charge/arrest records, followed by black female cases (26.4%). While black female cases had the highest percentage of sex related charges/arrests (4.9%), black male cases had the highest percentage (24.2%) of drug related charges/arrests.

Figure 4. Percentage of P & S Syphilis Cases That Had Charge/Arrest Records by Type of Charge/Arrest, Race and Gender, Nashville, TN, 1994-1998
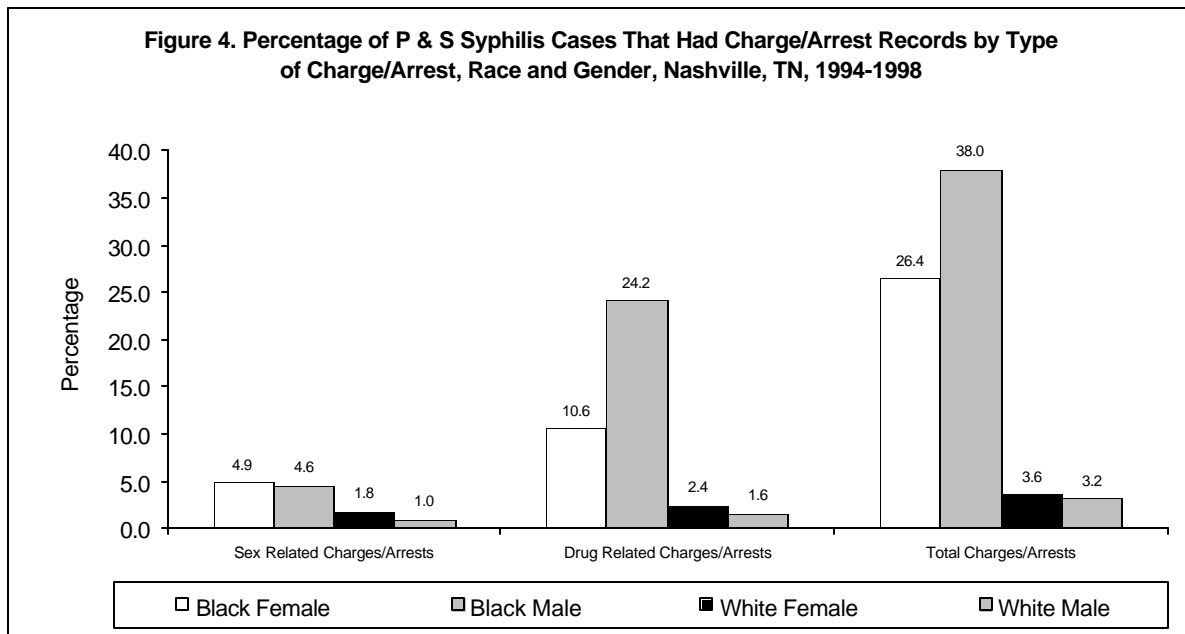
d.   Pre-epidemic versus epidemic

It is noted that while the number of cases increased more than three times from the pre-epidemic period (1994-1995) to the epidemic period (1996-1998), the percentage of the cases with charge/arrest records increased proportionally as well (Table 2). For total charge/arrests, the percentage of the cases increased more than three times. For sex related charge/arrests, the percentage of the cases increased almost three times. For drug related charge/arrests, the percentage of the cases increased more than three times.

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Table 2. Number and Percentage of P & S Syphilis Cases That Had Criminal Charge/Arrest Records by Type of Charge/Arrest, Stage of Syphilis, Pre-Epidemic and Epidemic Period, Nashville, TN, 1994-1998

	Sex Related Charges/Arrests (% in parenthesis) Cases/year in 2nd line	Drug Related Charge/Arrest (% in parenthesis) Cases/year in 2nd line	Total Charge/Arrests (% in parenthesis) Cases/year in 2nd line	Total Cases (% in parenthesis)
Pre-epidemic (1994-1995)	26 (3.2%) 13 cases/year	72 (9.0%) 36 cases/year	136 (17%) 68 cases/year	196 (24.4%)
Epidemic (1996-1998)	73 (9.1%) 24.3 cases/year	240 (29.9%) 80 cases/year	438 (54.6%) 146 cases/year	606 (75.6%)
Primary Syphilis	30 (3.7%)	116 (14.5%)	186 (23.2%)	240 (29.9%)
Secondary Syphilis	69 (8.6%)	196 (24.4%)	388 (48.4%)	562 (70.1%)
Total	99 (12.3%)	312 (38.9%)	574 (71.6%)	802 (100%)

Furthermore, the number of cases who had charge/arrest records increased 114% from 68 cases/year during the pre-epidemic period to 146 cases/year during the epidemic period. The number of cases who had sex related charge/arrests per year increased 87% from 13 cases/year during the pre-epidemic period to 24.3 cases/year during the epidemic period. The number of cases who had drug related charge/arrests increased 122% from 36 cases/year during the pre-epidemic period to 80 cases/year during the epidemic period (Table 2, Figures 5 and 6). These findings document an increased number of cases who engaged in sex and drug related activities during the epidemic period.

Figure 5. Percentage of P & S Syphilis Cases That Had Charge/Arrest Records, Pre-epidemic Period and Epidemic Period, Nashville, TN, 1994-1998
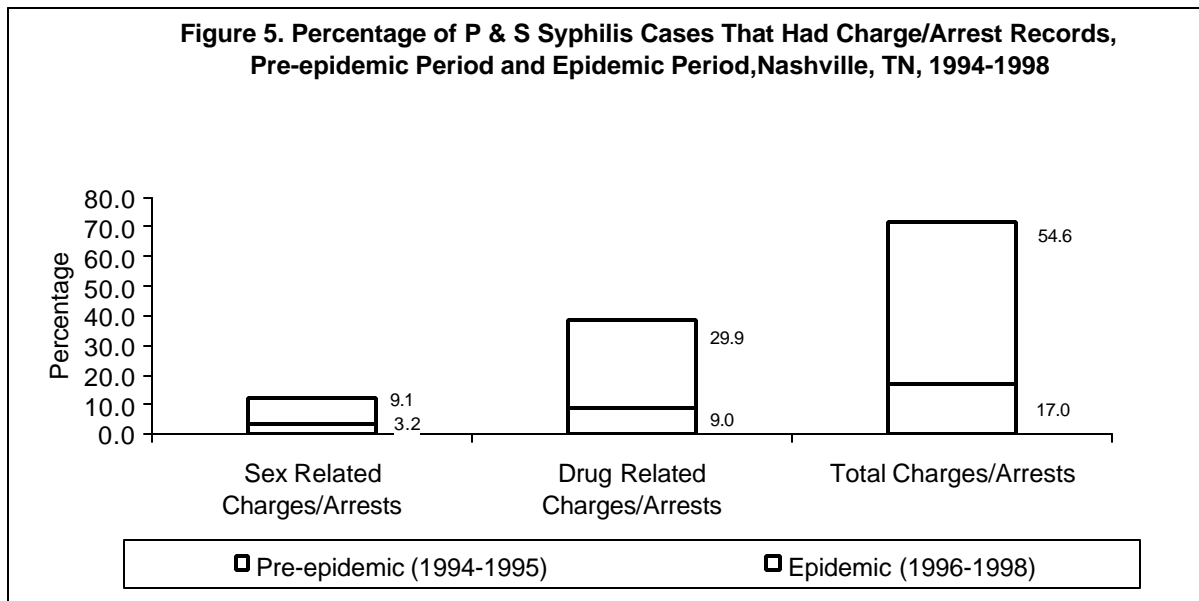
Figure 6. Number of P & S Syphilis Cases That Had Charge/Arrests Per Year by Type of Charge/Arrest, Pre-Epidemic Period and Epidemic Period, Nashville, TN, 1994-1998
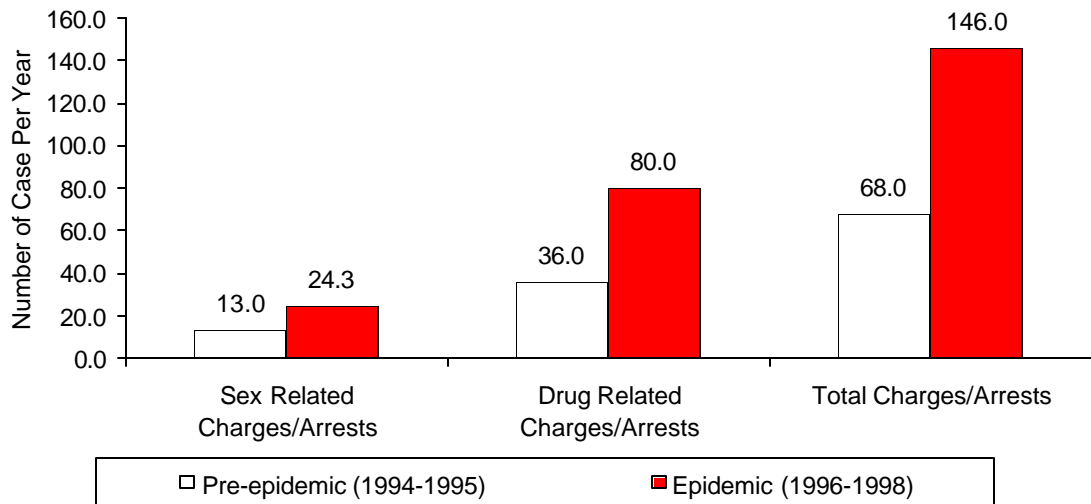
e. Stage of syphilis

Figure 7 demonstrates that syphilis cases in the secondary stage had a higher percentage (48.4%) of charges/arrests than those in the primary stage (23.2%). For sex related charges/arrests, the percentage of cases in the secondary stage who have charges/arrest records (8.6%) is more than twice higher than that in the primary stage (3.7%). For drug related charges/arrests, the percentage of cases in the secondary stage who had charges/arrest records (24.4%) is higher than that in the primary stage (14.5%).

Figure 7. Percentage of P & S Syphilis Cases That Had Charge/Arrest Records by Stage of Syphilis, Nashville, TN, 1994-1998
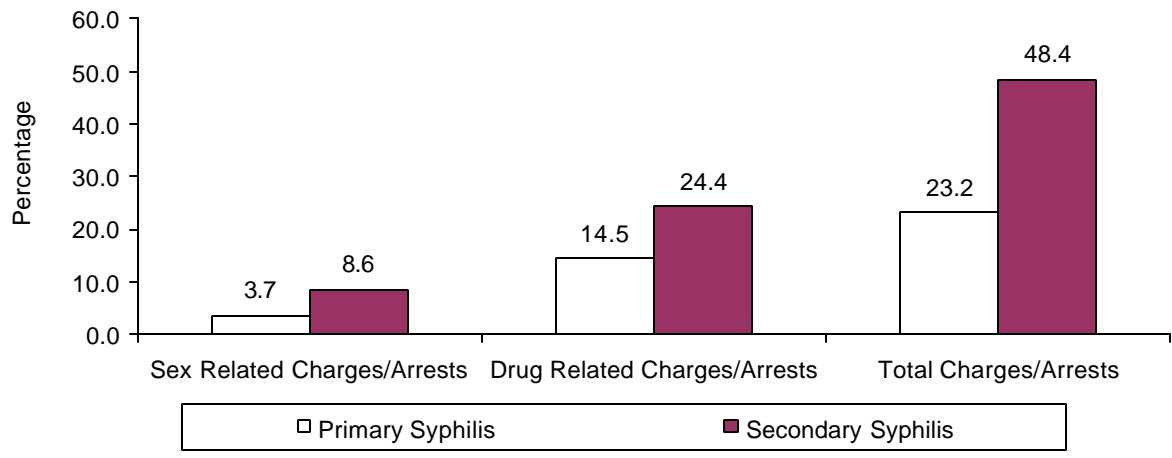
2.   Frequency of Charges Among Cases That Had Charge/Arrest Records

a.   Overview

For the cases who had charge/arrest records, it is important to assess the distribution of charges among the cases. Table 3 presents the number and percentage of criminal charges among reported P & S syphilis cases who had criminal charge/arrest records. There were 9,020 charges among the 574 cases who had criminal arrest records. On average, each of the 574 cases had 15.7 charg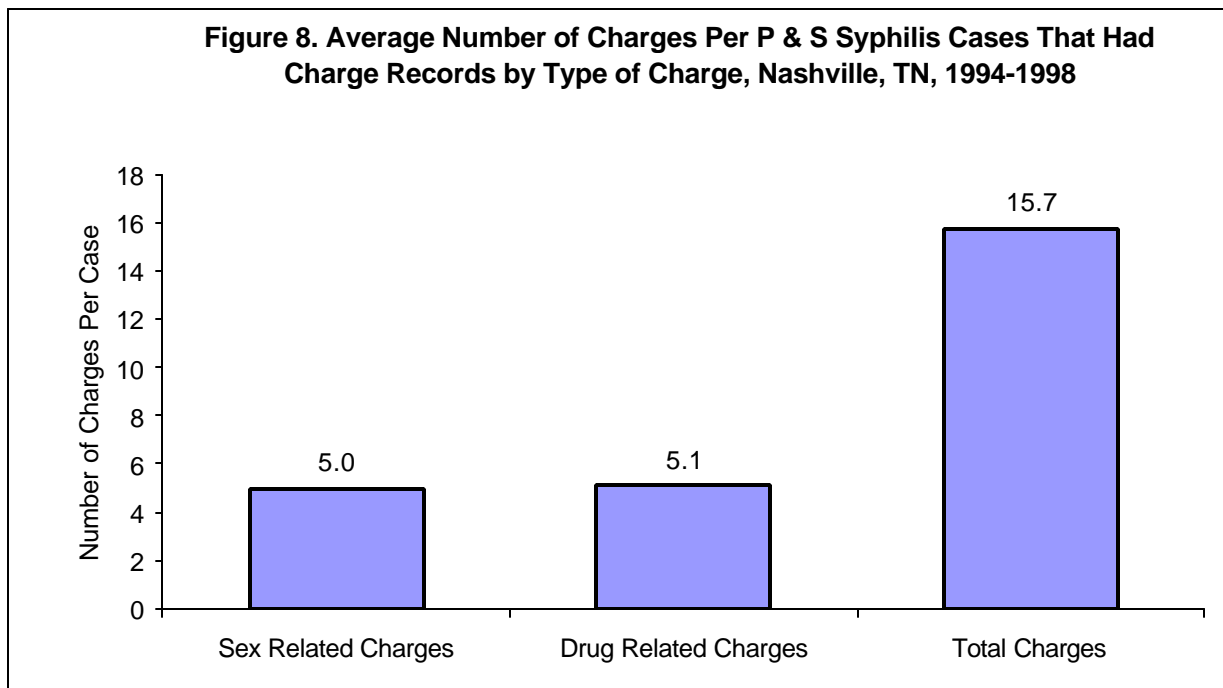es. For the 99 cases that had sex related charges/arrests, on average, each case had 5 sex related charges.   For the 312 cases that had drug related charges/arrests, on average, each case had 5.1 drug related charges, during his/her life time (Figure 8 on the next page). Of all charges among cases, 5.5% were sex related charges, 17.6% were drug related charges, and 76.9% were other charges.   As shown in Table 3, there is a statistically significant difference between gender for sex related charges and drug related charges. A statistically significant difference among races is also detected for sex related charges.

Table 3.   Number and Percentage of Criminal Charges Among P & S Syphilis Cases, Nashville, TN, 1994-1998

	Sex Related Charges		Drug Related Charges		Total Charges	
	#	%	#	%	#	%
Less than 20 Years	2	0.0	18	0.2	255	2.8
20-29 Years	131	1.5	388	4.3	2,510	27.8
30-39 Years	255	2.8	741	8.2	3,946	43.7
40-49 Years	96	1.1	355	3.9	1,910	21.2
50 + Years	10	0.1	87	1.0	399	4.4
Male	94**	1.0	1,109***	12.3	6,058	67.2
Female	400	4.4	480	23.0	2,962	32.8
Black	281*	3.1	1,360	15.1	7,815	86.6
White	213	2.4	227	2.5	1,197	13.3
Other	0	0.0	2	0.0	8	0.1
Black Female	208	2.3	347	3.8	2,183	24.2
Black Male	73	0.8	1,013	11.2	5,632	62.4
White Female	192	2.1	133	1.5	778	8.6
White Male	21	0.2	94	1.0	419	4.6
Other Female	0	0.0	0	0.0	1	0.0
Other Male	0	0.0	2	0.0	7	0.1
Total	494	5.5	1,589	17.6	9,020	100.0

Note: 1.   The percentages calculated in this table use 9,020 as the denominator.
2.   Comparisons between age group, gender, race, and gender/race: *$P<=0.05$, **$P<=0.01$, ***$P<=0.001$.
3.   Other refers to other races rather than black or white.

Figure 8. Average Number of Charges Per P & S Syphilis Cases That Had Charge Records by Type of Charge, Nashville, TN, 1994-1998

b.   Age

Figures 9 and 10 on the next page display that for syphilis cases who had criminal charge records, the 30-39 age group had the highest number of charge records (3,946 charges), accounting for 43.7% of all charges. On average, each case in the 30-39 age group had 17.1 charges. The 20-29 age group had the second highest number of charges (2,510 charges), followed by the 40-49 age group (1,910 charges).

For sex related charges, the 30-39 age group had the highest number of charge records (255 sex related charges), averaging 5 charges per case. The 20-29 age group had the second highest number of sex related charges (131 charges) and the highest number of sex related charges per case (6.2 sex related charges per case).

For drug related charges, the 30-39 age group had the highest number of charge records (741 drug related charges), averaging 5.1 charges per case. The 20-29 age group had the second highest number of sex related charges (388 charges) and the 40-49 age group had the highest number of drug related charges per case (5.5 drug related charges per case).

Figure 9. Number of Charges Among P & S Syphilis Cases by Type of Charge and Age Group, Nashville, TN, 1994-1998
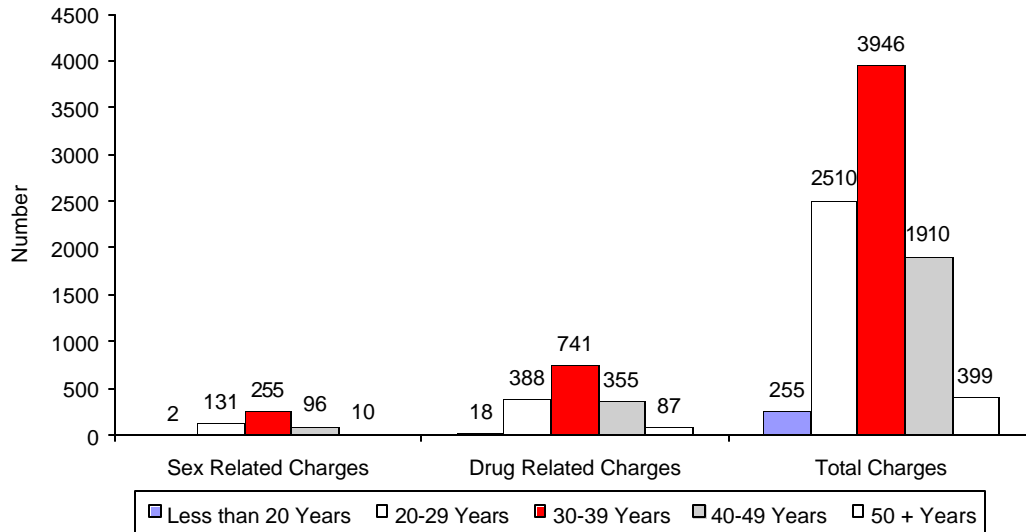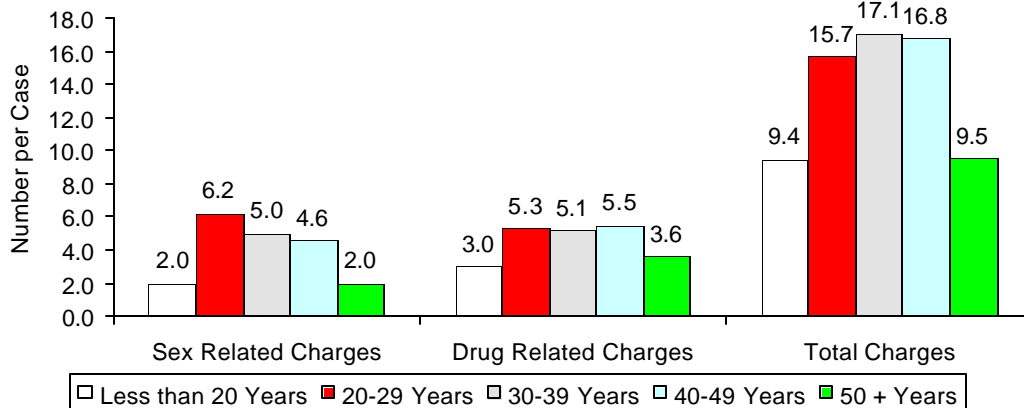

Figure 10. Number of Charges Per P & S Syphilis Cases That Had Charge Records by Type of Charge and Age Group, Nashville, TN, 1994-1998

c.   Gender and race

It is noted from Figure 11 that male P & S Syphilis cases who had charge records had more charges per case than female cases (male: 18.2; female: 12.2). However, for sex related charges, the female cases had more than three times higher the number of charges per case than male cases (male: 2.1; female: 7.4). For drug related charges, male cases had a slightly higher number of charges than their female counterparts (male: 5.3; female: 4.6). Racial discrepancies are also observed in Figure 11. White P & S syphilis cases who had charge records had a higher number of charges per case than their black counterparts (white: 21.8; black: 15.1). For sex related charges, white cases had more than twice the charges per case than black cases (white: 9.3; black: 3.7). For drug related charges, white cases had 45% higher number of charges per case than their black counterparts (white: 7.1; black: 4.9).

Figure 11. Number of Charges Per P & S Syphilis Cases That Had Charge Records by Gender and Race, Nashville TN, 1994-1998

Further examining the number of charges per case by gender and race (Figure 12 on the next page), it is found that white female P & S syphilis cases had the highest number of charges per case (26.8), followed by black males (18.5). For sex related charges, white female cases had the highest number of charges per case (12.8), followed by black female cases (5.3). For drug related charges, white male cases had the highest number of charges per case (7.2), followed by white female cases (7.0).
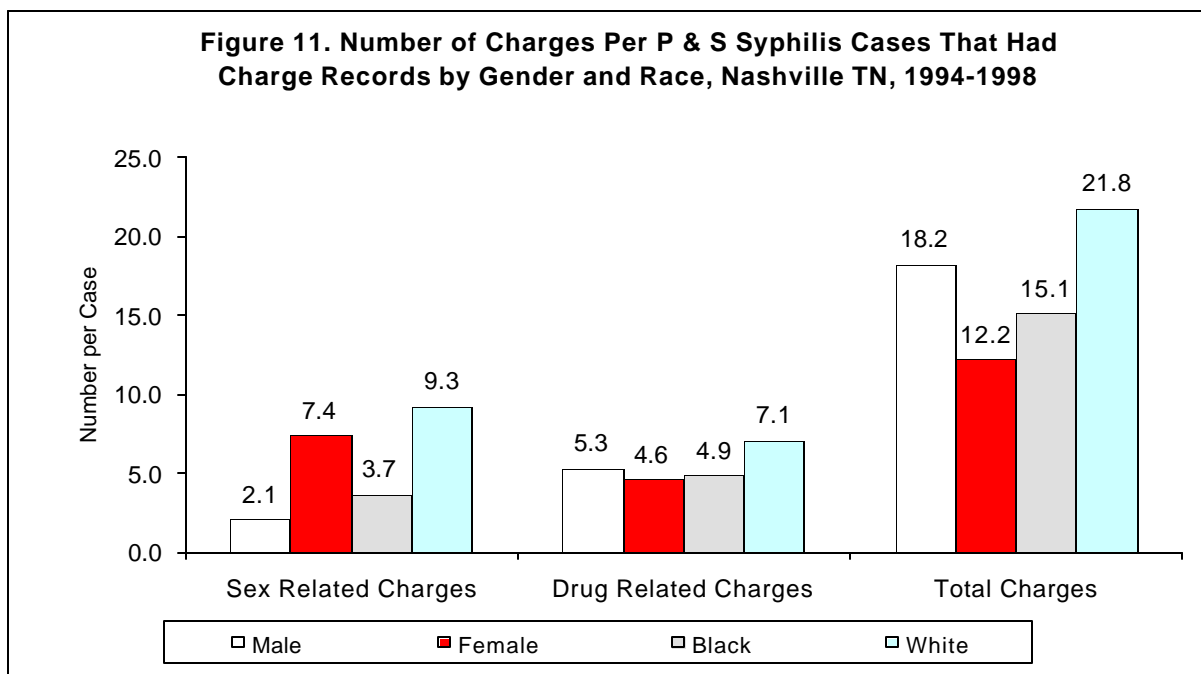
**Figure 12. Number of Charges Per P & S Syphilis Cases That Had
Charge Records by Race/Gender, Nashville, TN, 1994-1998**
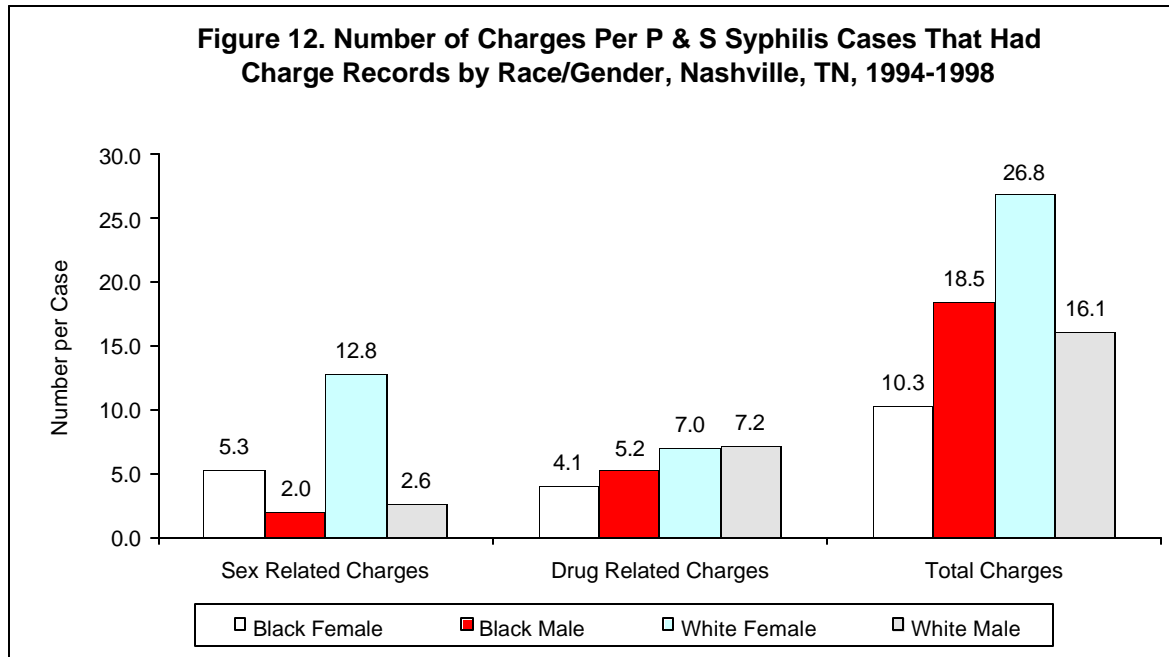
d.   Pre-epidemic versus epidemic

Table 4 on the next page presents the number and the percentage of reported P & S syphilis cases that had criminal charge records by type of charges and stage of syphilis during the pre-epidemic (1994-1995) and the epidemic period (1996-1998). Less than a quarter (22.2%) of charges occurred during the pre-epidemic period.   More than three quarters (77.8%) of charges occurred during the epidemic period. It is observed that the number of charges per year increased from the pre-epidemic period to the epidemic period. The number of total charges per year increased 233.1% from 1,002.5 charges per year during pre-epidemic period to 2,338.3 charges per year during the epidemic period. The number of sex-related charges per year increased 57.4% from 73.5 charges per year during the pre-epidemic period to 115.7 charges per year during the epidemic period.   The number of drug-related charges per year increased 261.3% from 161.5 charges per year during the pre-epidemic period to 422 charges per year during the epidemic period. Increases of sexual and drug-related charges per year among cases may reflect an increase of sexual and drug related activities in Nashville during the epidemic period.

Figure 13 reveals that overall the number of charges per P & S syphilis case increased 8.8% from the pre-epidemic period to the epidemic period (pre-epidemic: 14.7; epidemic 16.0). For sex related charges, the number of charges per case decreased 15.8% (pre-epidemic: 5.7; epidemic: 4.8).   For drug related charges, the number of charges per case increased 17.8% (pre-epidemic: 4.5; epidemic: 5.3).

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Table 4.   Number and Percentage of P & S Syphilis Cases That Had
Criminal Charge Records by Type of Charge, Stage of Syphilis,
Pre-Epidemic and Epidemic Period, Nashville, TN, 1994-1998

	Sex Related charges (charges/year in parenthesis)		Drug Related charges (charges/year in parenthesis)		Total charges (charges/year in parenthesis)	
	#	%	#	%	#	%
Pre-epidemic (1994-1995)	147 (73.5/year)	1.6	323 (161.5/year)	3.6	2,005 (1,002.5/year)	22.2
Epidemic (1996-1998)	347 (115.7/year)	3.8	1,266 (422.0/year)	14.0	7015 (2,338.3/year)	77.8
Primary Syphilis	88	1.0	591	6.6	3,190	35.4
Secondary Syphilis	406	4.5	998	11.1	5,830	64.6
Total	494	5.5	1,589	17.6	9,020	100.0

Figure 13. Number of Charges Per P & S Syphilis Cases That Had Charge Records By Type of Charge, Pre-epidemic Versus Epidemic, Nashville, TN, 1994-1998
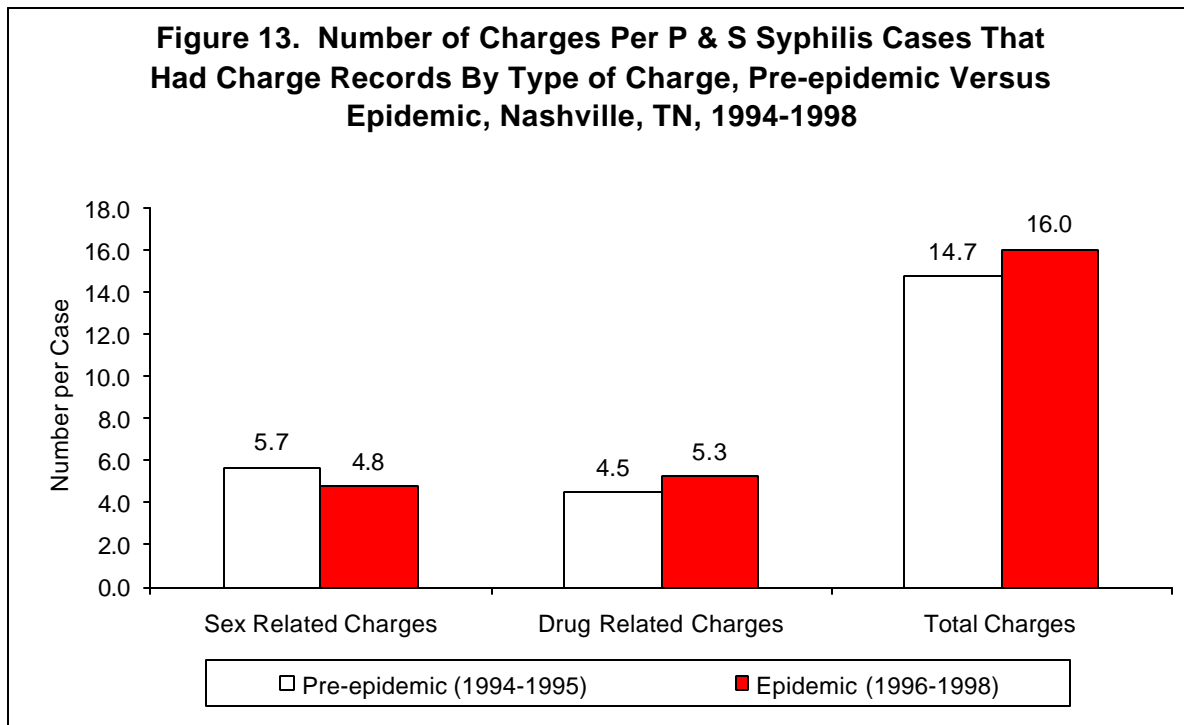
e.   Stage of syphilis

Figure 14 shows that more overall charges per case occurred during the primary stage of syphilis. However, for sex related charges, the number of charges per case among the secondary syphilis cases who had charges records were more than twice that of the primary syphilis cases (primary syphilis: 2.9;

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secondary syphilis: 5.9). For drug related charges, the number of charges for cases in the primary stage was the same as for cases in the secondary stage.

Figure 14. Number of Charges Per P & S Syphilis Cases That Had Charge Records by Type of Charge, Primary versus Secondary Syphilis, Nashville, TN, 1994-1998
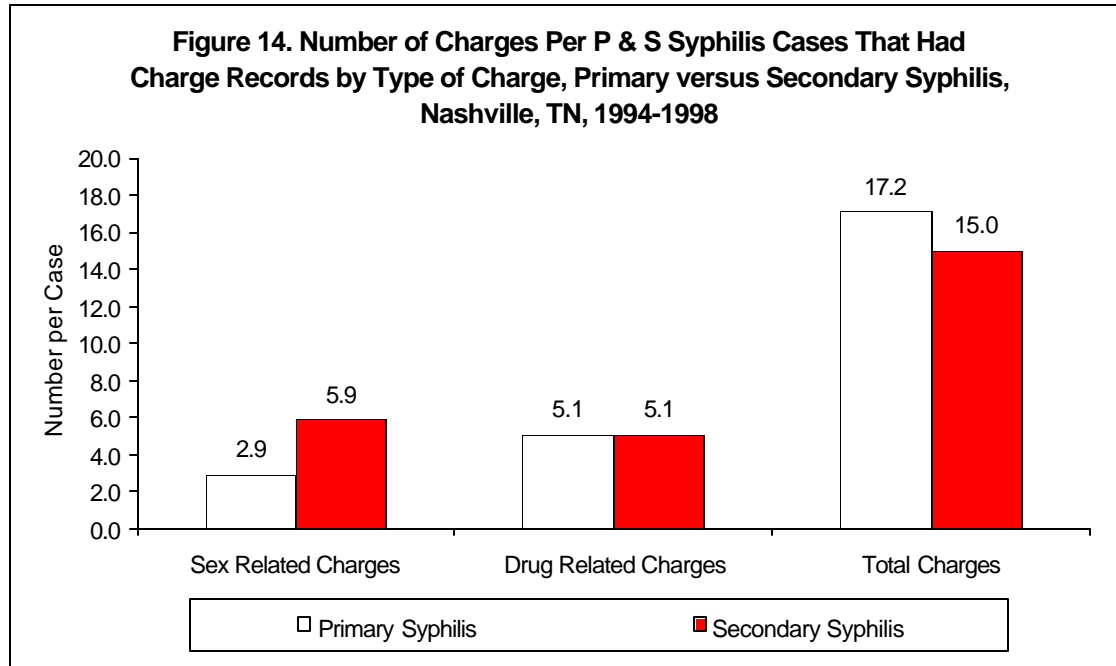
3.   Unmatched and Matched Case Control Groups

a.   Overview

A total of 802 P & S syphilis cases, 977 chlamydia controls, 1,354 gonorrhea controls, and 1,129 non-STD controls were selected into a series of three case control studies.

Table 5 presents demographic characteristics of cases and controls using unmatched data.   Significant differences among groups were detected in gender ($p < 0.001$) and race ($p < 0.001$). The differences in age between each pair (syphilis-chlamydia, syphilis-gonorrhea, syphilis-non-STD) are also significant at the 0.05 level. This suggests that gender, race, and age may be potential confounding factors. Therefore, it is appropriate to use matched data for further analysis.

Table 5. Demographic Characteristics of Cases and Controls (Unmatched Data), 1994-1998

Variable	Syphilis	Chlamydia	Gonorrhea	Non-STD
Total	802	977	1,354	1,129
Age (years)				
< 19	62 (7.7%)	187 (19.1%)	179 (13.2%)	106 (9.4%)
20 - 29	221 (27.6%)	413 (42.3%)	434 (32.1%)	365 (32.3%)
30 - 39	309 (38.5%)	303 (31.0%)	516 (38.1%)	416 (36.9%)
40 – 49	152 (19.0%)	66 (6.8%)	186 (13.7%	187 (16.6%)
≥ 50	58 (7.2%)	8 (0.8%)	39 (2.9%)	55 (4.9%)
Mean age	33.7 (SD=10.5)	27.6 (SD=8.1)	30.9 (SD=9.4)	32.2 (SD=9.7)
Gender				
Male	423 (52.7%)	429 (43.9%)	757 (55.9%)	477 (42.3%)
Female	379 (47.3%)	548 (56.1%)	597 (44.1%)	652 (57.8%)
Race				
Black	712 (88.8%)	880 (90.1%)	1,168 (86.3%)	918 (81.3%)
White	88 (11.0%)	95 (9.7%)	186 (13.7%)	211 (18.7%)
Other [*]	2 (0.2%)	2 (0.2%)	0 (--)	0 (--)

Note: 1.   * Other refers to other races including individuals who are not considered as black or white. One Asian and one Hispanic are included in the syphilis group, one Asian and one unknown race are included in the chlamydia group.

      2.   Significant differences among groups are detected in gender (p < 0.001) and race (p < 0.001), but not age. The overall mean age is 31 years (Standard Deviation (SD) = 9.66). The differences in age between each pair are significant at 0.05 level based on ANOVA test and pairwise comparison (With such a large sample size, it is easy to reach a significant level, though the actual differences may not necessarily be significant).

Table 6 presents demographic characteristics of matched case-control pairs. As can be seen, there is no significant difference in age, gender, and race between cases and controls after matching.

Table 6. Demographic Characteristics of Matched Case-Control Pairs, 1994-1998

Variable	Syphilis – Chlamydia (N = 659 pairs)		Syphilis – Gonorrhea (N = 764 pairs)		Syphilis – Non-STD (N = 784 pairs)	
	Case	Control	Case	Control	Case	Control
Age (years)						
Mean	30.8	30.2	32.8	32.6	33.5	33.5
S.D	8.3	8.0	9.6	9.4	9.9	9.9
Range	14 – 63	13 – 61	14 – 72	14 – 69	14 – 74	16 - 72
Gender						
Male	309 (46.9%)		408 (53.4%)		407 (51.9%)	
Female	350 (53.1%)		356 (46.6%)		377 (48.1%)	
Race						
Black	593 (90.0%)		685 (89.7%)		696 (88.8%)	
White	65 (9.9%)		79 (10.3%)		88 (11.2%)	
Other [*]	1 (0.2%)		0 (--------)		(------)	

Note: * Other refers to other races rather than black or white. In this case, other is an Asian.

Table 7 displays the number of cases and controls that had charge/arrest records during different periods of time cumulatively.

Table 7.   Distribution of Charge/Arrest History by Time and Case Control Pairs, 1994-1998

Time Prior to (After *) Disease Diagnosis	Syphilis – Chlamydia (n=659 pairs)		Syphilis – Gonorrhea (n=764 pairs)		Syphilis – Non-STD (n=784 pairs)	
	Case	Control	Case	Control	Case	Control
Sex Related Charges/Arrests						
in 5 weeks*	9 (1.37%)	4 (0.61%)	9 (1.18%)	7 (0.92%)	9 (1.15%)	0 (----)
< 1 mon	3 (0.46%)	1 (0.15%)	4 (0.52%)	4 (0.52%)	4 (0.51%)	0 (----)
< 6 mon	23 (3.49%)	6 (0.91%)	25 (3.27%)	8 (1.05%)	26 (3.32%)	6 (0.77%)
< 1 yr	32 (4.86%)	6 (0.91%)	34 (4.45%)	12 (1.57%)	36 (4.59%)	9 (1.15%)
< 2 yrs	45 (6.83%)	12 (1.82%)	47 (6.15%)	16 (2.09%)	48 (6.12%)	11 (1.40%)
< 3 yrs	52 (7.89%)	15 (2.28%)	54 (7.07%)	20 (2.62%)	54 (6.89%)	14 (1.79%)
< 4 yrs	55 (8.35%)	16 (2.43%)	57 (7.46%)	23 (3.01%)	57 (7.27%)	15 (1.91%)
< 5 yrs	63 (9.56%)	17 (2.58%)	67 (8.77%)	25 (3.27%)	69 (8.80%)	18 (2.30%)
> 5 yrs	77 (11.68%)	24 (3.64%)	91 (11.91%)	42 (5.50%)	93 (11.86%)	32 (4.08%)
All time	79 (11.99%)	26 (3.95%)	93 (12.17%)	42 (5.50%)	95 (12.12%)	32 (4.08%)
Drug Related Charges/Arrests						
in 5 weeks*	44 (6.68%)	13 (1.97%)	48 (6.28%)	32 (4.19%)	47 (5.99%)	0 (----)
< 1 mon	18 (2.73%)	13 (1.97%)	20 (2.62%)	18 (2.36%)	20 (2.55%)	0 (----)
< 6 mon	58 (8.80%)	35 (5.31%)	64 (8.38%)	41 (5.37%)	65 (8.29%)	43 (5.48%)
< 1 yr	85 (12.90%)	53 (8.04%)	95 (12.43%)	63 (8.25%)	97 (12.37%)	72 (9.18%)
< 2 yrs	129 (19.58%)	64 (9.71%)	143 (18.72%)	103 (13.48%)	146 (18.62%)	88 (11.22%)
< 3 yrs	154 (23.37%)	75 (11.38%)	173 (22.64%)	131 (17.15%)	175 (22.32%)	96 (12.24%)
< 4 yrs	170 (25.80%)	82 (12.44%)	193 (25.26%)	152 (19.90%)	197 (25.13%)	110 (14.03%)
< 5 yrs	186 (28.22%)	93 (14.11%)	214 (28.01%)	167 (21.86%)	218 (27.81%)	122 (15.56%)
> 5 yrs	247 (37.48%)	122 (18.51%)	294 (38.48%)	220 (28.80%)	301 (38.39%)	172 (21.94%)
All time	251 (38.09%)	123 (18.66%)	299 (39.14%)	223 (29.19%)	307 (39.16%)	175 (22.32%)
Other Charges/Arrests	453 (68.74%)	319 (48.41%)	528 (69.11%)	479 (62.70%)	537 (68.49%)	387 (49.36%)
Total Charges/Arrests	471 (71.47%)	329 (49.92%)	549 (71.86%)	488 (63.87%)	562 (71.68%)	397 (50.64%)

Note: Charges/Arrest history is cumulative. Percentages were calculated using "n" in the table.

b.   Univariate analysis

Preliminary univariate analysis revealed that the number of syphilis cases who had a sex related charge/arrest history was statistically significantly higher than that of chlamydia controls in all time charges/arrests, charges/arrests of five-plus years before the diagnosis date, and in charges/arrests of less than 1 month before the diagnosis date. The number of syphilis cases who had drug related charges/arrests was statistically significantly higher than that of chlamydia controls in all time charges/arrests and charges/arrests of five-plus years before the diagnosis date (Table 8 on page 25).

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No statistically significant relationship was found between syphilis cases and sex related charge/arrest records when compared with the gonorrhea control group. However, the number of syphilis cases who had drug-related charges/arrests is statistically significantly higher than that of gonorrhea controls in all time charges/arrests, charges/arrests of five-plus years before the diagnosis date, and in charges/arrests of 1-6 months before the diagnosis date (Table 9 on page 26).

For the syphilis and non-STD matches, the number of syphilis cases that had sex related charges/arrests was statistically significantly higher than that of non-STD controls in only charges/arrests of 3-4 years before the diagnosis date. The number of syphilis cases that had drug related charges/arrests was statistically significantly higher than that of non-STD controls in only charges/arrests of five-plus years before the diagnosis date (Table 10 on page 27).

Table 8. Number of Cases/Controls (Syphilis/Chlamydia) that Had Charge/Arrest Records, Odds Ratio (OR), and 95% Confidence Interval (CI), 1994-1998

		Chlamydia									
		Sex Related Charges/Arrests[1]					Drug Related Charges/Arrests				
Time Prior to Disease Diagnosis	Syphilis	Yes[4]	No[5]	Total	OR[6]	95% CI[7]	Yes[8]	No[9]	Total	OR	95% CI
In 5 Weeks After Diagnosis	Yes[2]	0	9	9	7.56	0.38 - 150.53	0	44	44	0.50	0.03 - 8.58
	No[3]	4	646	650			13	602	615		
	Total	4	655	659			13	646	659		
< 1 mon	Yes	0	3	3	**62.43**	**2.15 - 1812.75**	0	18	18	1.26	0.07 - 21.98
	No	1	655	656			13	628	641		
	Total	1	658				13	646			
1 – 6 mon	Yes	0	22	22	2.56	0.14 - 47.64	1	46	47	0.56	0.07 - 4.22
	No	5	632	637			23	589	612		
	Total	5	654				24	635			
6 mon – 1 yr	Yes	0	12	12	NA[10]	NA	1	40	41	0.65	0.09 - 4.91
	No	0	647	647			23	595	618		
	Total	0	659				24	635			
1 – 2 yrs	Yes	1	23	24	4.56	0.53 - 39.42	1	64	65	0.41	0.05 - 3.06
	No	6	629	635			22	572	594		
	Total	7	652				23	636			
2 – 3 yrs	Yes	0	16	16	5.55	0.28 - 111.74	2	53	55	1.23	0.28 - 5.44
	No	3	640	643			18	586	604		
	Total	3	656				20	639			
3 – 4 yrs	Yes	0	9	9	22.79	0.87 - 596.08	1	46	47	0.68	0.09 - 5.18
	No	1	649	650			19	593	612		
	Total	1	658				20	639			
4 – 5 yrs	Yes	0	12	12	17.24	0.67 - 444.26	2	34	36	1.54	0.35 - 6.78
	No	1	646	647			23	600	623		
	Total	1	658				25	634			
> 5 yrs	Yes	6	71	77	**2.65**	**1.02 - 6.89**	58	189	247	**1.67**	**1.12 - 2.48**
	No	18	564	582			64	348	412		
	Total	24	635				122	537			
All time	Yes	7	72	79	**2.87**	**1.17 - 7.07**	58	193	251	**1.59**	**1.07 - 2.36**
	No	19	561	580			65	343	408		
	Total	26	633	659			123	536	659		

Note: 1. Charge/Arrest history is not cumulative except for "All Time".   2. "Yes" refers to sex or drug related charges/arrests. 3. "No" indicates that there were no sex or drug related charges/arrests. 4. "Yes" refers to sex related charges/arrests. 5. "No" indicates that there were no sex related charges/arrests. 6. "OR" refers to the matched case-control odds ratio. ORs are adjusted for the "time prior to disease diagnosis" strata. 7. "CI" refers to the confidence interval for the OR. 8. Yes refers to drug related charges/arrests. 9. "No" indicates that there were no drug related charges/arrests. 10. "NA" indicates not applicable.

Table 9.   Number of Cases/Controls (Syphilis/Gonorrhea) that Had Charge/Arrest Records, Odds Ratio (OR), and 95% Confidence Interval (CI), 1994-1998

| Time Prior to Disease Diagnosis | Syphilis | Gonorrhea | | | | | | | | | |
| | | Sex Related Charges/Arrests[1] | | | | | Drug Related Charges/Arrests | | | | |
		Yes[4]	No[5]	Total	OR[6]	95% CI[7]	Yes[8]	No[9]	Total	OR	95% CI
In 5 Weeks After Diagnosis	Yes[2]	0	9	9	5.25	0.28 - 98.70	3	45	48	1.58	0.46 - 5.38
	No[3]	7	748	755			29	687	716		
	Total	7	757	764			32	732	764		
< 1 mon	Yes	0	4	4	18.68	0.87 - 400.45	0	20	20	0.96	0.06 - 16.45
	No	4	756	760			18	726	744		
	Total	4	760				18	746			
1 – 6 mon	Yes	0	23	23	3.49	0.18 - 66.65	5	46	51	**3.58**	**1.29 - 9.93**
	No	4	737	741			21	692	713		
	Total	4	760				26	738			
6 mon – 1 yr	Yes	0	13	13	6.15	0.32 - 120.03	1	47	48	0.54	0.07 - 4.08
	No	4	747	751			27	689	716		
	Total	4	760				28	736			
1 – 2 yrs	Yes	0	24	24	2.31	0.13 - 42.10	5	69	74	0.99	0.38 - 2.58
	No	6	734	740			47	643	690		
	Total	6	758				52	712			
2 – 3 yrs	Yes	0	15	15	3.69	0.20 - 68.42	4	57	61	1.23	0.42 - 3.56
	No	6	743	749			38	665	703		
	Total	6	758				42	722			
3 – 4 yrs	Yes	0	8	8	6.79	0.35 - 130.39	7	51	58	2.35	1.0 - 5.51
	No	6	750	756			39	667	706		
	Total	6	758				46	718			
4 – 5 yrs	Yes	0	13	13	5.03	0.27 - 95.53	2	41	43	0.90	0.21 - 3.87
	No	5	746	751			37	684	721		
	Total	5	759				39	725			
> 5 yrs	Yes	5	86	91	1.0	0.38 - 2.61	101	193	294	**1.54**	**1.12 - 2.12**
	No	37	636	673			119	351	470		
	Total	42	722				220	544			
All time	Yes	5	88	93	0.97	0.37 - 2.54	104	195	299	**1.55**	**1.13 - 2.13**
	No	37	634	671			119	346	465		
	Total	42	722	764			223	541	764		

Note: 1. Charge/Arrest history is not cumulative except for "All Time".   2. "Yes" refers to sex or drug related charges/arrests. 3. "No" indicates that there were no sex or drug related charges/arrests. 4. "Yes" refers to sex related charges/arrests. 5. "No" indicates that there were no sex related charges/arrests. 6. "OR" refers to the matched case-control odds ratio. ORs are adjusted for the "time prior to disease diagnosis" strata. 7. "CI" refers to the confidence interval for the OR. 8. "Yes" refers to drug related charges/arrests. 9. "No" indicates that there were no drug related charges/arrests.

Table 10.   Number of Cases/Controls (Syphilis/Non-STD) that Had Charge/Arrest Records, Odds Ratio (OR), and 95% Confidence Interval (CI), 1994-1998

Time Prior to Disease Diagnosis	Syphilis	Non-STD									
		Sex Related Charges/Arrests[1]					Drug Related Charges/Arrests				
		Yes[4]	No[5]	Total	OR[6]	95% CI[7]	Yes[8]	No[9]	Total	OR	(95%CI)
In 5 Week After Diagnosis	Yes[2]	0	9	9	NA[10]	NA	0	47	47	NA	NA
	No[3]	0	775	775			0	737	737		
	Total	0	784	784			0	784	784		
< 1 mon	Yes	0	4	4	NA	NA	0	20	20	NA	NA
	No	0	780	780			0	764	764		
	Total	0	784				0	784			
1 – 6 mon	Yes	1	23	24	6.57	0.74 - 58.47	2	50	52	0.67	0.16 - 2.87
	No	5	755	760			41	691	732		
	Total	6	778				43	741			
6 mon – 1 yr	Yes	0	14	14	7.56	(0.37 – 153.16)	2	47	49	0.70	0.17 - 2.99
	No	3	767	770			42	693	735		
	Total	3	781				44	740			
1 – 2 yrs	Yes	0	23	23	6.46	(0.30 – 138.41)	3	72	75	1.10	0.32 - 3.71
	No	2	759	761			26	683	709		
	Total	2	782				29	755			
2 – 3 yrs	Yes	0	15	15	7.07	(0.35 – 142.68)	1	59	60	0.54	0.07 - 4.08
	No	3	766	769			22	702	724		
	Total	3	781				23	761			
3 – 4 yrs	Yes	0	9	9	**27.18**	**(1.04 – 710.69)**	1	59	60	0.46	0.06 - 3.41
	No	1	774	775			26	698	724		
	Total	1	783				27	757			
4 – 5 yrs	Yes	0	16	16	6.63	(0.33 – 133.53)	2	41	43	1.29	0.30 - 5.61
	No	3	765	768			27	714	741		
	Total	3	781				29	755			
> 5 yrs	Yes	4	89	93	1.06	(0.37 – 3.11)	78	223	301	**1.45**	**1.03 - 2.04**
	No	28	663	691			94	389	483		
	Total	32	752				172	612			
All time	Yes	5	90	95	1.36	(0.51 – 3.63)	79	228	307	1.38	0.98 - 1.93
	No	27	662	689			96	381	477		
	Total	32	752	784			175	609	784		

Note: 1. Charge/Arrest history is not cumulative except for "All Time".   2. "Yes" refers to sex or drug related charges/arrests. 3. "No" indicates that there were no sex or drug related charges/arrests. 4. "Yes" refers to sex related charges/arrests. 5. "No" indicates that there were no sex related charges/arrests. 6. "OR" refers to the matched case-control odds ratio. ORs are adjusted for the "time prior to disease diagnosis" strata. 7. "CI" refers to the confidence interval for the OR. 8. "Yes" refers to drug related charges/arrests. 9. "No" indicates that there were no drug related charges/arrests. 10. "NA" indicates not applicable.

c.   Multivariate analysis

A further multivariate analysis using a logistic regression model and continuous variables found a statistically significant relationship between P & S syphilis cases and criminal charge/arrest records. Specifically, sex related criminal behavior (reflected by sex related charges) increased the risk of the acquisition of syphilis (Table 11 on page 29 and Table 12 on page 30).

(1)   Logistic regression analysis using unmatched data

Table 11 presents the results of logistic regression analysis using unmatched data. Four logistic regression models were built using: 1) syphilis cases and all three groups of controls (Model A), 2) syphilis cases and chlamydia controls (Model B), 3) syphilis cases and gonorrhea controls (Model C), and 4) syphilis cases and non-STD controls (Model D).

In the logistic regression Model A analysis that included the entire study sample of 4,262 subjects (cases and controls), age, race, sex related charges and drug related charges were found to be statistically significant. Based on the model estimation, each additional year in age increased the odds of the syphilis acquisition by 3.3% ((exp(0.0324) - 1) x 100). As compared to other races, the risk for blacks to acquire syphilis was about 1.6 times of that for other races (mainly whites in this study) (OR 1.57, 95% CI 1.22, 2.02). For sex related charges, each additional charge may increase the risk by 30.1%. For drug related charges, each additional charge may increase the risk by 4.0%.

When only the risk between syphilis cases and chlamydia controls was compared (Logistic Regression Model B), the age risk effect doubled from 3.3% in Model A to 7.0% in Model B. The effect of race was insignificant (not shown in Table 19). The risk effect of sex related charges increased slightly to 35.0%. The risk effect of drug related charges was insignificant (not shown in Table 19). The risk effect of other charges increased by 1.9%.

When only the risk between syphilis cases and gonorrhea controls was compared (Logistic Regression Model C), the age risk effect increased by 3.3%. As compared to males, the risk for females to acquire syphilis was higher (OR 0.79, 95% CI 0.65, 0.95). As compared to other races, the risk for blacks to acquire syphilis was about 1.5 times of that for other races (there are mainly whites in this study) (OR 1.48, 95% CI 1.11, 1.96). The risk effect of sex related charges increased by 22.2%. The risk effect of drug related charges and other charges was insignificant (not shown in Table 19).

When only the risk between syphilis cases and non-STD controls was compared (Logistic Regression Model D), age effect was insignificant (not shown in Table 19). As compared to females, the risk for males to acquire syphilis was 1.3 times higher than that of females (OR 1.33, 95% CI 1.09, 1.62). As compared to other races, the risk for blacks to acquire syphilis was about 2 times of that for other races (mainly whites in this study)

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(OR 2.02, 95% CI 1.52, 1.2.68). The risk effect of sex related charges increased by 82.6% for each additional sex related charge. The risk effect of drug related charges increased by 5.3% for each additional drug related charge. The risk effect of other charges increased by 1.1% for each additional other charge.

Table 11.   Results of Logistic Regression Analysis Using All Study Subjects (Cases and Controls) (Unmatched Data)

Variable	Parameter (β) Estimate	Odds Ratio (95% CI)	p - Value	Estimated % Changes in risk per unit increase[2]
Logistic Regression Model A. Syphilis and all controls (n = 4,262)				
Age	0.0324	1.03 (1.03 - 1.04)	< 0.0001	3.3
Race	0.4524	1.57 (1.22 - 2.02)	0.0004	N/A
Sex related charges	0.2628	1.30 (1.19 - 1.42)	< 0.0001	30.1
Drug related charges	0.0393	1.04 (1.02 - 1.06)	0.0003	4.0
Logistic Regression Model B. Syphilis and Chlamydia controls (n = 1,779)				
Age	0.0675	1.07 (1.06 - 1.08)	< 0.0001	7.0
Sex related charges	0.3003	1.35 (1.16 - 1.58)	< 0.0001	35.0
Other charges	0.0192	1.02 (1.01 - 1.03)	< 0.0001	1.9
Logistic Regression Model C. Syphilis and Gonorrhea controls (n = 2,156)				
Age	0.0326	1.03 (1.02 - 1.04)	< 0.0001	3.3
Gender	-0.2407	0.79 (0.65 - 0.95)	0.0122	N/A
Race	0.3887	1.48 (1.11 - 1.96)	0.0069	N/A
Sex related charges	0.2001	1.22 (1.11 - 1.34)	< 0.0001	22.2
Logistic Regression Model D. Syphilis and Non-STD controls (n = 1,931)				
Gender	0.2818	1.33 (1.09 - 1.62)	0.0056	N/A
Race	0.7019	2.02 (1.52 - 2.68)	< 0.0001	N/A
Sex related charges	0.6021	1.83 (1.48 - 2.25)	< 0.0001	82.6
Drug related charges	0.0513	1.05 (1.01 - 1.09)	0.0085	5.3
Other charges	0.0111	1.01 (1.00 - 1.02)	0.0394	1.1

Note: 1.   Presented in the table are variables that are significant based on the forward stepwise selection. All subjects (cases and controls) in each defined case-control group were included in the analysis. Each model included six variables: three demographic variables - age (years of age), gender (male/female), race (black/non-black), and three types of charges - sex-related charges (all records), drug-related charges (all records), other charges (all records).

2.   % change = 100 (exp(β) - 1), a negative value indicates a reduction in risk.

3.   N/A: Not applicable because race and gender are not continuous variables.

4.   CI: Confidence Interval.

(2)   Logistic regression analysis using matched data

To control for the potential confounding effects of demographic factors, a conditional logistic estimation procedure was performed using case control pairs matched by age (± 3years), gender, and race. Each analysis included three types of criminal charges (sex related charges, drug related charges, and other charges). Results of the conditional logistic regression analysis are presented in Table 12 on the next page.

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Sex related charges remained statistically significant in all matched groups. It's estimated that the risk of syphilis acquisition increased 16.7% per additional sex related charges in the syphilis-gonorrhea matched pairs to 62.6% per additional sex related charges in syphilis-non-STD matched pairs.

For drug related charges, the risk increased 4.9% when comparing the risk between syphilis cases and non-STD controls. However, the effect of drug related charges was insignificant when comparing the risk between syphilis cases and chlamydia controls and syphilis cases and gonorrhea controls.

For other charges, the risk increased 2.1% for each additional charge when comparing the risk between syphilis cases and chlamydia controls. The risk increased 1.0% for each additional charge when comparing the risk between syphilis cases and non-STD controls, although it was only marginally significant (p=0.08). The effect of other charges was insignificant when comparing the risk between syphilis cases and gonorrhea controls.

Table 12.   Results of Logistic Regression Analysis Using Matched Data

Variable	Parameter (β) Estimate	Odds Ratio (95% CI)	p - Value	Estimated % Changes in risk per unit increase[2]
Logistic Regression Model A: Syphilis - Chlamydia Matches (n = 659 pairs)				
Sex related charges	0.3776	**1.46 (1.19 - 1.79)**	0.0003	45.9
Other charges	0.0205	1.02 (1.01 - 1.03)	< 0.0001	2.1
Logistic Regression Model B: Syphilis and Gonorrhea controls (n = 764 pairs)				
Sex related charges	0.1545	**1.17 (1.06 - 1.29)**	0.0020	16.7
Logistic Regression Model C: Syphilis and non-STD controls (n = 784 pairs)				
Sex related charges	0.4858	**1.63 (1.31 - 2.02)**	< 0.0001	62.6
Drug related charges	0.0480	1.05 (1.01 - 1.09)	0.0210	4.9
Other charges	0.0100	1.01 (1.00 - 1.02)	0.0839	1.0

Note: 1.   Presented in the table are variables that are significant based on the forward stepwise selection. Only matched cases and controls in the defined case-control groups were included in the analysis. Each model included three types of charges – sex related charges (all records), drug related charges (all records), other charges (all records).
2.   Percentage change = 100 (exp(β) - 1), a negative value indicates a reduction in risk.
3.   Other charges are the criminal charges other than sex and drug related charges.
4.   CI: Confidence Interval.

The same analyses were also performed for the pre-epidemic period and the epidemic period. A similar conclusion was reached for the epidemic period. The result for the pre-epidemic period was slightly different due to the small number effect.

C.   Discussion

Previous studies showed that women incarcerated on drug or prostitution charges had higher rates of syphilis (5-15%) (21). This study found that syphilis cases had a higher percentage of criminal charges on sex or drug related

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offenses (sex: 12.3% of the cases; drug: 38.9% of the cases), reaffirming an association between syphilis occurrence and illegal sex or drug related activities.

This study also documents that there was an increased number of cases who engaged in sex and drug related activities during the epidemic period (sex: a 87% increase from 13 cases/year during the pre-epidemic period to 24.3 cases/year during the epidemic period; drug: a 122% increase from 36 cases/year to 80 cases/year), suggesting that sex and drug related behaviors may play a role in this syphilis epidemic.

In addition, the study found that the number of charges per year increased during the epidemic period (sex: a 57% increase from 73.5 charges per year during the pre-epidemic period to 115.7 charges per year during the epidemic period; drug: a 261% increase from 161.5 charges per year to 422 charges per year). Increases of sex and drug related charges among cases during the epidemic period may reflect the increase of sex and drug related activities in Nashville during the epidemic period.

The study reveals that the 30-39 age group had the highest percentage of cases who engaged in illegal drug or sex related activities (sex related charges/arrests: 6.4%, drug related charges/arrests: 18%). Given the fact that the 30-39 age group had the highest incidence rate in this epidemic (6), it is likely that illegal drug or sex related activities in the 30-39 age group may have contributed to Nashville's syphilis epidemic.

Furthermore, the finding that secondary syphilis cases had a higher percentage of sex and drug related charges/arrests (sex: 8.6%, drug: 24.4%) and the fact that more sex related charges occurred among secondary syphilis cases who had charge/arrest records may represent a missed opportunity for syphilis prevention. Some of these illegal drug and sex related activities may occur during the primary stage of syphilis, the most infectious period, spreading syphilis to the community.

The series of case-control studies found that there was a statistically significant association between syphilis and sex related charges. The risk of syphilis acquisition increased within an estimated range of 16.7% to 62.6% per each additional sex related charge and increased 4.9% per each additional drug related charge.

Given the fact that there were 99 P & S syphilis cases that had sex related charge/arrest records (Table 1 on page 9) with 494 sex related charges (Table 3 on page 15) and 312 cases that had drug related charge/arrest records with 1,589 drug related charges, the opportunities for these cases to spread syphilis in Nashville are substantial.

In addition, even though the studies found a substantial risk of syphilis acquisition related to criminal activities, this risk is likely underestimated due to underreporting bias. In other words, the risk of acquisition of syphilis would be higher if underreporting bias was eliminated.

Not all sex and drug related crime behaviors result in criminal charges or arrests. Furthermore, there is a lack of sensitivity in matching names. For instance, many STD cases use different names. Because they may have a different identity for different purposes, a search of the criminal arrest database may not match these as the same person. The database may contain nicknames and variations of names. Although the address, race, age, and gender identifiers were used to address the issue, the matching results are very likely lower than the actual numbers.

It is recognized that underreporting bias exists in the data system. Although the law requires every syphilis case to be reported, it is not the case in practice. Due to different reporting practices in public and private sectors, it is possible that some cases are not reported. The unreported cases are not available for inclusion in the study. Sex and drug related crime behavior by unreported syphilis cases may not be the same as the reported cases. The effect of case underreporting is to be determined. A further assessment of underreporting and/or misdiagnosis of P & S syphilis patients should shed light on this issue.

Besides underreporting bias, other possible limitations of this study are recall bias, misclassification bias, and the confounding effect.

Recall bias, common in case control studies, is not an issue of concern in this study. This is because 1) the data used in this study are routinely collected by government agencies, 2) a standard data abstract form was used to ensure the consistency of data abstraction, 3) the procedures to abstract data and of quality assurance are well documented, 4) very specific definitions are established in the syphilis surveillance system and in the criminal charge/arrest data system, and 5) comprehensive implementation and quality assurance procedures are established in the agencies. Therefore, data obtained for this study should be regarded as among the most reliable data.

Cases have very clearly defined national diagnosis criteria. Misdiagnosis error will have very little effect on the outcome of the study. Because disease status and exposure data were from the existing public health surveillance system and legal system, ascertainment of disease and exposure status were ensured. Therefore, misclassification bias should have little or no effect on the association.

Using chlamydia and gonorrhea cases as controls increased the similarity of cases and controls. Many intangible selection factors that identified syphilis

cases would be the same for chlamydia and gonorrhea cases. However, they may share the same risk behaviors as syphilis cases, leading to an underestimate of the relationship between syphilis and sex and drug related behaviors. To control this bias, a non-STD control group was selected from non-STD clinic visitors. The regression analysis results suggested that this bias does exist but its impact was not substantial. A risk effect for sex related charges was detected in all three regression models (syphilis-chlamydia, syphilis-gonorrhea, syphilis- non-STD). The highest risk effect was detected in syphilis-non-STD comparison (OR: 1.63), followed by syphilis-chlamydia comparison (OR: 1.46). The lowest risk effect was detected in syphilis gonorrhea comparison (OR: 1.17). These results are consistent with the previous study findings in which gonorrhea patients reported cocaine use and sex with prostitutes nearly as frequently as did syphilis patients (11).

A series of matched case control studies with a multivariance logistic regression analysis reduces the possibility of confounding effects of gender, race, and age. However, this study was not able to control for other confounders such as socio-economic factors.

In summary, sex and drug related behaviors evidenced by sex and drug related charges/arrests are associated with acquisition of syphilis. The risk effect is significant in sex and drug related charges even after controlling for confounding factors, that is, the risk of syphilis acquisition increased 16.7% to 62.6% per additional sex related charge and increased 4.9% per additional drug related charge. Based on this series of studies, it is very likely that the increased illegal sex and drug related activities among cases during the epidemic period are at least partially responsible for Nashville's current syphilis epidemic.